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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/990,087	11/20/2001	Stephen G. Sligar	87-00	1280

23713 7590 06/11/2003

GREENLEE WINNER AND SULLIVAN P C  
5370 MANHATTAN CIRCLE  
SUITE 201  
BOULDER, CO 80303

EXAMINER

LI, RUIXIANG

ART UNIT

PAPER NUMBER

1646

DATE MAILED: 06/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/990,087	<b>Applicant(s)</b> SLIGAR ET AL.	
	<b>Examiner</b> Ruixiang Li	<b>Art Unit</b> 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 24 April 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-36 is/are pending in the application.
- 4a) Of the above claim(s) 11, 12 and 20-36 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-7, 9, 10 and 13 is/are rejected.
- 7) ☒ Claim(s) 8 and 14-19 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 20 November 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
 If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) ☐ All   b) ☐ Some \*   c) ☐ None of:  
 1. ☐ Certified copies of the priority documents have been received.  
 2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
 \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
 a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                  | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)         | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other:  |

**DETAILED ACTION*****Election/Restrictions***

1. Applicants' election with traverse of Group I, claims 1-19, directed to SEQ ID NO: 17, in Paper No. 7 filed on April 24, 2003 is acknowledged. Applicants also elected the species integral membrane protein in claim 13. The traverse is on the ground that neither the membrane scaffold protein nor the DNA molecules encoding it are found in nature. There is no other purpose for the claimed DNA molecules other than for expression of the membrane scaffold proteins. A search of the protein, at least in the scientific literature, should be expected to uncover any references to the encoding DNA molecules. This has been fully considered but is not deemed to be persuasive because (i) a membrane scaffold protein does exist in nature, e.g., apo A-I protein (see, e.g., bottom of page 2 to top of page 3 of specification); (ii) Groups I and IV are drawn to entirely different products; (iii) search and consideration constitutes undue burden on the office.

Applicants argue that Groups I and IV (including newly added claim 36) are related to the technical features of the membrane scaffold proteins and request the simultaneous examination of all the species of the membrane scaffold proteins of the present invention, the DNA molecules encoding them, recombinant host cells and methods of producing the membrane scaffold proteins. This has been fully considered but is not deemed to be persuasive because the restriction requirement

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for U.S. applications is different from the practice of lack of unity for PCT. For a U.S. application, inventions can be restricted as long as they are distinct and constitute an undue burden on the office, as is the case here.

With respect to the membrane protein species election requirement, Applicants argue that the membrane scaffold proteins act in a common way to support the hydrophobic protein in a nanoscale particle. This has been fully considered but is not deemed to be persuasive because each of the three membrane proteins is a distinct chemical entity, and has a distinct structure from the other, and each requires a separate search of the prior art.

Regarding the sequence election, Applicants submit that sequences are species within the genus of membrane scaffold protein. The Examiner notes that the sequence election requirement in Paper No. 6 is not a species election, rather, it sets forth further invention groups.

The requirement is still deemed proper and is therefore made FINAL.

2. Applicants' amendment in Paper No. 7 has been entered in full. Claim 29 has been amended. Claim 36 has been added. Claims 1-36 are pending. Claims 1-10 and 13-19 are under consideration. All other claims are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention (claims 11 and 12 are withdrawn from consideration due to species election).

***Priority***

3. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. 119(e) to a provisional application, 60/252,233, filed on November 20, 2000.

***Drawings***

4. The drawings filed on November 20, 2001 are accepted the Examiner.

***Rejections—35 USC § 101***

5. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claims 1-7 and 9 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter, a membrane scaffold protein and a nanoscale particle comprising the membrane scaffold protein. Since a membrane scaffold protein, e.g., apo A-I protein, and a nanoscale particle comprising apo A-I protein, e.g., a particle of high-density lipoproteins (HDL) can be found in nature (see e.g., bottom of page 2 to top of page 3 of specification), the claims read on a product of nature. Products of nature do not constitute statutory subject matter. It is suggested that the word "a synthetic membrane scaffold protein" or "an artificial membrane scaffold protein" be used in claim 1 to overcome this rejection.

***Claim Rejections—35 USC § 102***

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-7, 9, 10, and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Bayburt et al. (Journal of Structural Biology 123:37-44, 1998).

Bayburt et al. teach reconstitution and imaging of an integral membrane protein, NADPH-cytochrome P450 reductase in a nanometer-size phospholipid bilayer. This nanobilayer consists of an approximately 10-nm-diameter circular (discoidal) phospholipid domain stabilized by apolipoprotein A1, an amphipathic membrane scaffold protein (See, e.g., Abstract), which forms  $\alpha$ -helices (top of right column of page 37).

Furthermore, the membrane scaffold protein taught by Bayburt et al, by its nature, would form a nanoscale particle as recited in the claims in the presence of amphipathic lipid molecules (e.g., cholesterol, and glycolipids) other than phospholipids. Therefore, the reference of Bayburt et al. meets the limitations of claims 1-7, 9, 10, and 13.

***Claim Objections—Minor Informalities***

9. Claims 1 and 4 are objected to because of typographic errors: “ora” (claim 1, line 2) should be “or a”; “selfassembles” (claim 4, line 2) should be “self assembles”.

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10. Claims 8, 18, and 19 are objected to because they recite unelected subject matter, amino acid sequences (SEQ ID NOS: 6, 9, 19, 23, 29, 43-45).

11. Claims 14-17 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Appropriate correction is required.

12. The prior art made of record in PTO-892 form and not relied upon is considered pertinent to applicant's disclosure.

#### ***Advisory Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (703) 306-0282. The examiner can normally be reached on Monday-Friday, 8:30 am-5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for this Group is (703) 305-3014 or (703) 308-4242.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [yvonne.eyler@uspto.gov].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record

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includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.



Ruixiang Li  
Examiner  
June 8, 2003